Blood-Stream Infection (CDC)

From: Lewis, Steve [Steve.Lewis@CareFusion.com]
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To: Blood-Stream Infection (CDC)
Subject: Response to Draft Guidelines for the Prevention of Intravascular Catheter-Related Infections

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Guidelines for Prevention of Intravascular Catheter-Related Infection -2009 Draft
http://wwwn.cdc.gov/publiccomments/
http://edocket.access.gpo.gov/2009/pdf/E9-26393.pdf

Thank you for the opportunity to comment on the proposed guidelines.

76 Category II. Suggested for implementation and supported by suggestive clinical or
77 epidemiologic studies or a theoretical rationale.
78 Unresolved issue. Represents an unresolved issue for which evidence is insufficient or no

Line 1612 6. When needleless systems are used, the split septum valve is preferred over the Line 1613 mechanical valve due to increased risk of infection [336-339]. Category II

As an infusion system manufacturer, CareFusion offers both types of needle-free IV Connectors – luer activated valves and split septum connectors. The new guidance document encourages the use of needle-free IV connectors. However, it suggests a preference for split septum devices based on Class II evidence supported by four retrospective epidemiological studies. This recommendation seems unwarranted from both the discussion and literature cited and gives more weight to uncontrolled observational studies than both the earlier and three recent randomized prospective clinical studies with contrary conclusions.

Casey AL et al. "Infection risks associated with needleless devices."[1]

Casey and Elliot[1] a published a meta-analysis in 2007 combining the results from five prospective trials. They showed that none of the 5 prospective randomized trials published prior to 2007 had any significant increase in colonization rates. The combined odds ratio reported for contamination was 0.6 with a 95% confidence interval of 0.5-0.7. Three of the 5 studies actually showed reduced colonization rates. Three of the studies examined catheter-related bloodstream infection as an outcome [Bouza, Lucet, and Yebenes].[2,3,4] The combined results from these three randomized studies using bloodstream infection as the endpoint was 0.4 with a 95% confidence interval of 0.2-0.9.
Three further *prospective, randomized clinical studies* include:

Garcia R., et al. A Study of the Effects on Bacteremia and Sharps Injury Rates after introduction of an Advanced Luer Activated Device for Intravascular Access in a large Hospital Setting.[5]

In this study, needle stick injury (NSI) and catheter-related bloodstream infection (CR-BSI) were evaluated during use of both split septum connectors (SSC) and a luer activated device (LAD). The study was conducted as a 3 month pre-post evaluation with a strong monitored education program implemented for all clinicians. There was a 3 month period using split septum devices, followed by a 3 month period of using LADs. In the SSC group there were 203 patients with 2,566 catheter days and 3 BSIs. In the LAD group there were 212 with 2,612 catheter days and 3 BSIs. The risk ratio was 106 (0.22-5.19 95% confidence interval, p=0.69). Beyond no statistical difference being found in infection rates between the two devices, NSI injuries were reduced from 4 in the SSC group to zero in the LAD group.

Phillips, A. et al., A Comparison of Bloodstream Infection Rates in Children with Two Different Types of Injection Caps in Use on Central Venous Catheters.[6]

This abstract describes a prospective, paired sample, non-blind comparison study between split septum connectors and SmartSite® valves (purchased through Medex) in pediatric intensive care and medical surgical units. With 287 patients allocated by surname assignment, they found 8 BSIs in 1265 catheter days in the SmartSite® group and 5 BSIs in 1076 catheter days in the split septum group (p = 0.79), risk ratio 1.36 (0.44-4.2) Although the overall BSI rates were lower than those reported in other studies, these did not show a difference between the devices.

Schilling, et al; 'The Impact of needleless connector device design on central venous catheter occlusion in children: A Prospective, controlled trial".[7]

In this prospective, randomized study three connector types were evaluated for catheter occlusion and infection rates – split septum connectors, SmartSite® valve and positive pressure luer activated valve. The study concluded that luer activated valves were more effective in reducing catheter occlusion than split septum connectors. Complete occlusion rates were 12.7% for the split septum devices vs. 1.3% using the SmartSite® device ($p < 0.001$). Catheter related BSI rates were not significantly different. Lower infection rates were observed with the luer activated valves flushed with saline solution compared with the split septum connectors also flushed with heparin solution but were not statistically significant.

In 2006 Neil-Weise[8] et al published a systematic review of the randomized trials related to needleless closed catheter access. Six studies were found. Table 2 in their study shows the risk ratios with 95% confidence intervals for the varied outcomes is shown below. Across the 13 outcomes reported, only two have relative risks greater than one. Most show reductions in 30-50% range favoring needleless devices.

Table II Summary estimates of associations between treatment and control groups expressed as relative risk (RR) and 95% confidence intervals (CI) using a random-effects model

Study	Needleless closed system	Conventional open system	RR (95% CI)
CRBI			
Bouza *et al.*, 2003[10]	6/178	11/174	0.53 (0.20-1.41)
Lucet *et al.*, 2000[12]	1/70	1/67	0.96 (0.06-14.99)
Yebenes *et al.*, 2004[13]	1/139	7/139	0.14 (0.02-1.15)
Patients with at least one CRBI			
Bouza *et al.*, 2003[10]	6/178	9/174	0.65 (0.24-1.79)
Catheter tip colonization			
Bouza *et al.*, 2003[10]	94/865	156/909	0.63 (0.50-0.80)
Lucet *et al.*, 2000[12]	17/70	13/67	1.25 (0.66-2.37)
Yebenes *et al.*, 2004[13]	9/139	13/139	0.69 (0.31-1.57)
Hub inlet colonization			
Bouza *et al.*, 2003[10]	12/279	46/324	0.30 (0.16-0.56)
Casey *et al.*, 2003[11,a]	1/91	17/102	0.07 (0.01-0.49)
Casey *et al.*, 2003[11,b]	9/91	22/102	0.46 (0.22-0.94)
Casey *et al.*, 2003[11,c]	8/92	16/102	0.55 (0.25-1.23)
Lucet 2000[12]	22/235	15/216	1.35 (0.72-2.53)
Skin colonization			
Bouza et al., 2003[10]	66/279	110/324	0.70 (0.54-0.90)

CRBI, catheter-related bloodstream infection.
[a] Comparison I with 0.5% chlorhexidine in gluconate 70% isopropyl alcohol as disinfectant.
[b] Comparison II with 70% alcohol as disinfectant.
[c] Comparison III with 10% aqueous povidione-iodine as disinfectant.

The combined evidence cited above suggest that a recommendation opposite to the that made in lines 1612 and 1613 could be made at the Category IB level if not the Category IA level. The factor that no doubt tempers such a recommendation are the data from the 4 problematic single center observational studies cited in the guideline [336-339] and described below.

Maragakis LL, et al. "Increased Catheter-Related Bloodstream Infection Rates After the Introduction of a New Mechanical Valve Access Port"[9]

In the report by Maragakis et al, a 60% increase in infection rates in the ICUs was reported with the introduction of SmartSite® valve.[9] The increase that was associated with one ICU was statistically **insignificant**. However, data was pooled from multiple sources with unknown times of introduction of SmartSite® valve to gain statistical significance. Even more troubling is that while they point to SmartSite® valve as the cause of the increase in BSI from 4/1/04-12/6/04 with a return to near baseline by 3/31/05, they fail to address that during a similar period from 1/1/03 to 12/31/03 they experienced an over 2 fold increase in CR-BSI/1000 catheter days in those same units that had not returned to baseline by 3/31/04 which was approximately when SmartSite was introduced. To blame one peak in BSI on SmartSite® valve in one year when the previous year they also experienced a similar increase when SmartSite® valve was not in use creates questions regarding the validity of the study's conclusions. In neither period was actual compliance with recommendations for catheter care measured, nor was there any control for risk of CR-BSI which is known to vary between NICU patients based on patient weight and the proportion of patients in other ICU settings.

Salgado CD, et al. "Increased Rate of Catheter-Related bloodstream Infection Associated With Use of a Needleless Mechanical Valve Device at a Long-Term Acute Care Hospital" [10]

The article retrospectively describes the experience of Kindred Hospital in South Carolina with SmartSite® valves and Interlink split septum caps.

The authors' state," Education on proper use and disinfection of the needleless mechanical valve device (NMVD) was provided to healthcare personnel by nurse educators from the hospital and representatives from the manufacturer." The article further provides the following:
"The IV tubing (including needleless device) was routinely changed every 96 hours unless blood (or blood products) or parental nutrition was administered". The recommended manufacturer's change protocol for valves and IV set with valves is 72 hours or 100 activations. Thus, the valves were not changed per manufacturer's recommendations.

When the institution began experiencing difficulty, CareFusion, formerly Cardinal Health, dispatched an Intravenous Nurse Specialist at the request of the institution to do re-education. She determined that in-servicing had been done by the in house Education Department alone. During a unit-to-unit walk through, it was determined that they were using a combination of B Braun and Alaris IV pumps, Ultrasite, InterLink and SmartSite® valve. On some patients, it was observed InterLink being attached to SmartSite® valve, as well as SmartSite® valve attached to SmartSite® valve. This was not because the valves were leaking, but rather because the staff didn't know how to properly use the product. In addition, there was extremely rapid turnover in this extended care facility that provides care for long term patients, many of whom are immune-compromised. Rapid turnover alone has been shown to be a cause of increased BSI[11]. The use of three different connectors with different directions for use simultaneously during a study that was supposed to implicate increased infections due to one of the three is not credible.

Rupp *ME, et al "Outbreak of Bloodstream Infection Temporally Associated with the Use of an Intravascular Needleless Valve" [12]*

Dr. Rupp reported an increase in infection with Smartsite.[11] In the only comparable data presented (BSI/1000 catheter days in the ICU), he fails to address the 4 fold increase that occurred from September 04-November 04 and attempts to explain the failure of the rate to fall by noting that administrative issues lead to failure to purge existing stock. This is a hypothetical argument that suffers from the ecologic fallacy. Only if the persistent high rates could be explicitly tied to infections in cases using unpaged stock could this argument have casual implications. See Figure 1 Below:

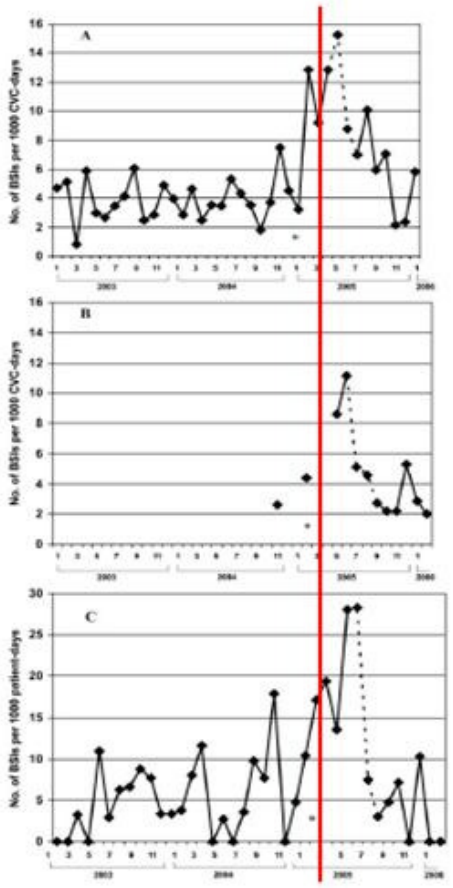

Figure 1. Rate of bloodstream infection versus time, January 2003 to February 2006. Numbers 1–12 in the x-axis refer to consecutive months (from January to December) of the year indicated. Bloodstream infections in critical care units (*A*), in inpatient nursing units (*B*), and in cooperative care units (*C*). Infections are expressed as bloodstream infections (BSI) per 1000 central venous catheter (CVC)–days in panels *A* and *B* and as bloodstream infections per 1000 patient-days in panel *C*. *Asterisk*, when the positive-pressure displacement valve was introduced; *dotted trend line*, the transition period as the valves were removed from clinical use. In panel *B*, the first 2 data points indicate separate observation months in November 2004 and February 2005; continuous surveillance was instituted in May 2005. The connector valve was introduced in late February 2005 and was completely removed from clinical use by September 2005.

Unfortunately, as seems often to be the case, there is no accounting of the adherence of practice to evidence or remediation efforts other than it was reported that "The intravenous set and connector valves were changed every 7 days" The recommended manufacturer's change protocol for valves is 72 hours or 100 activations. No attempt was made to determine if failure to follow manufacturer's instructions was an issue. This is particularly important since Rupp pointed out that "in one instance, it was noted that the broth was bloody after being flushed through the connector." This suggests that the catheters may not have been flushed properly, a known cause for increased BSI with mechanical valves.

Field K, et al. "Incidence of Catheter-Related Bloodstream Infection Among Patients With a Needleless Mechanical Valve-Based Intravenous Connector in an Australian Hematology-Oncology Unit. Infection Control and Hospital Epidemiology; May 2007:28(5):610-613.[13]

These authors from an oncology unit in Australia reported a rise in BSI rates from 2.6 infections per 1000 catheter days to 5.8 infections per 1000 catheter days. The rate ratio ranged from 1.6 to 3.2 across varied hematologic and oncologic conditions. As in other reports coagulase negative staphylococci comprised a majority of the cases. However, in this study there was a nearly 6 month lag time between introduction and the reported spike. This time course is not at all like that reported by Rupp again raising concerns as to whether this is an effect of the valve or some other related events such as how the valves are being managed.

It is of note that in 2008 there was a review of all IV connectors currently on the market by ECRI, a non-profit, independent consumer organization.[14] In their review, they noted that:

"This analysis by ECRI noted human factors and starting on page 262 of the supplement note: the information in the literature does not conclusively demonstrate that the new needleless connectors are responsible for changes in infection rate, nor do published reports clearly point to any one type or model of NC as being more susceptible to increasing CR-BSI rates than any other. The report did not support one technology over the other and listed split septum as 'less preferred' based on the increased potential to use needles resulting in caregiver needle stick injuries with the same rates of CR-BSI between the devices."[14]

The major risks of BSI associated with needleless valves are:

1. Failure to properly disinfect the surface of the connector before IV access.
2. Not flushing connectors properly after use
3. Not changing connectors according to protocol and other policy violations
4. Not using or clamping the extension set properly

In retrospective studies the authors often claim there was no change in practice during the study period. It is in fact necessary to change practice when new technology is introduced in order to prevent errors in use. In addition none of the studies actually audit practice to determine compliance with current policy or adjust for risk of CR-BSI in varied patient populations i.e. NICU vs. Pediatric ICU vs. adult ICU.

The measures and the process measures outlined in the study by Pronovost are essential for preventing CR-BSI.

> ***Pronovost P, Needham D, Berenholtz S, Sinopoli D, Chu H, Cosgrove S, Sexton B, Hyzy R, Welsh R, Roth G, Bander J, Kepros J, Goeschel C. An intervention to decrease catheter-related bloodstream infections in the ICU.[15]***

Probably the best example of the interventions required to markedly decrease and maintain low CR-BSI rates is the Keystone ICU collaborative. 108 ICUs from 70 hospitals have participated in a 2 year collaborative directed by the Michigan Hospital Association and the Johns Hopkins University Quality and Safety Research Group. Pronovost et al. presented data that the median rate of catheter related bloodstream infection per 1000 catheter days decreased from 2.7 infections at baseline to 0 infections at 3 months after intervention and the mean rate decreased from 7.7/1000 at baseline to 1.4/1000 at 16-18 months of follow up. This required a sustained, multi-intervention collaborative. First, unit based safety programs were introduced with daily goal sheets. Removal of catheters was discussed on daily rounds. Each unit had a physician and nurse champion who reviewed data regularly, participated in conference calls every other week, and attended state wide meetings twice a year. They were responsible for disseminating information to the rest of the ICU staff. The evidence based procedures recommended by the CDC to prevent CR-BSI were introduced over the next 3 months as well as strategies to improve compliance such as central line carts and check lists. After 3 months the median infection rate was 0 which has been sustained for 15 months**. "All types of participating hospitals realized a similar improvement."[15] It is known to us that 4 institutions that use luer activated needleless valves for peripheral and central lines were participating hospitals. It is likely that other institutions used the luer activated valves as well.**

Current market share of needle-free systems that are available on the market today; based on IMS data through December 2008[16] indicates 74% of the market utilizes luer access devices of one kind or another in comparison to 26% of the market that utilize a split septum system. We have seen a continuing decline in split septum connector usage over the past 2 to 3 years.

Many institutions have selected luer access devices over split septum injection sites, for reasons such as the following:

- Luer access devices provide a passive system; this provides a higher level of needle-free compliance and reduces the potential for continued use of needles and incurring needle stick injuries.
- Eliminates the need for safety pieces such as caps, cannulas, and other add-on pieces. This reduces both excess inventory and additional cost.
- A luer lock connection provides a more secure connection and reduces the potential for accidental luer disconnections.

Marilyn Hanchett, RN, PhD remarks "some manufacturers have attempted to leverage infection concerns to better position their individual brands." "There is simply not enough scientifically rigorous evidence upon which to make a conclusion. Although there have been sporadic reports of increased infections, there is insufficient evidence to indicate a trend that can be reliably associated with a specific type of connector or any particular product."[17]

It is of deep concern that, except for Dr. Heard, no actual or potential conflicts of interest past or present were acknowledged by authors of these guidelines. For this report, Dr. Rupp may be conflicted in this recommendation as he indicated being a paid consultant and member of the speaker's bureau of Becton Dickinson in his 2007 publication in Clinical Infectious Disease[11] (336). The study cited as evidence in this guideline (336) was funded by Becton Dickinson and the author, Dr.

Rupp, was and may still be on the speaker's bureau of that vendor. In fact, Dr. Rupp's study is listed as the number one reference on Becton Dickinson's marketing material for their Interlink split septum device. The FDA has been criticized for undue influence from clinicians with close ties, whether current or remote, to vendors during the approval process for a device or drug. Similarly, the possibility of a conflict of interest playing a role in national guidelines endorsed by a government agency is at least as, if not more, worrisome and may merit further investigation by the societies participating in the guidelines, congress, and the media.

To conclude, CareFusion submits an objection to the acceptance of

Line 1612 When needleless systems are used the split septum valve is preferred over the
Line 1613 mechanical valve due to increased rate of infection. [336-339] Category II

As stated in the ECRI 2008 publication, "no single design, model, or manufacturer of NC has been consistently associated with unusually high CR-BSI rates. And until more consistent and informative data is available, a conclusive link between specific NCs and increased CR-BSI rates cannot be established."

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Sincerely,

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